UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,046	02/03/2004	Brian Hague	CP246	2324

27573 7590 06/22/2006

CEPHALON, INC.
41 MOORES ROAD
PO BOX 4011
FRAZER, PA 19355

EXAMINER	
VANIK, DAVID L	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,046	HAGUE ET AL.	
	Examiner	Art Unit	
	David L. Vanik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-105* is/are pending in the application.

4a) Of the above claim(s) *6-10,12-14,26 and 44-105* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11,15-25 and 27-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/13/04; 9/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicant's Response to Election/Restriction filed on 2/8/2006.

Election/Restrictions

Applicant's election with traverse of Claims 1-43 in the reply filed on 2/8/2006 is acknowledged. The traversal is on the ground(s) that examining the compositions of Group II, Claims 44-95, and the methods of Groups III-VI, Claims 96-104, would not place a burden on the examiner. The examiner respectfully disagrees with this assertion and respectfully submits that Groups III-VI are distinct from group I for the reasons set forth in the 1/9/2006 restriction requirement. With respect the composition claims of Group II (Claims 44-95), because they do not contain an element that is essential and fundamental to Group I (Claims 1-42), that is, a buffer present in a sufficient amount to maintain a portion of a pharmaceutical agent, upon dissolution of said agent in salvia, in an unionized state, the claim set of Group II is patentably distinct from Group I. The examiner respectfully asserts that Applicant recognizes this distinction in categorizing Group II as having three essential elements (a composition comprising (1)fentanyl and (2) an excipient, (3) wherein the composition is essentially sugar-free), while categorizing Group I as comprising four essential elements (a composition comprising (1)an ionizable pharmaceutical agent, (2) a buffer, (3) an excipient, (4) wherein the composition is essentially sugar-free).

The election of species consistent with Example 6 of the instant specification is acknowledged. As such, isomalt was elected from the "excipient" group, fentanyl was selected as the pharmaceutical agent to be examined, and citric acid – di-sodium hydrogen phosphate was chosen from the "buffer" category. Because the cited references teach sorbitol as the sugar-substitute, the claims encompassing the limitation "sorbitol" (as an individual polyhydric alcohol and not as a combination) will be rejoined and examined (Claim 5). As a result of the restriction/species elections the following claims will be examined: 1-5, 11, 15-25, 27-43. As such, claims 6-10, 12-14, 26, and 44-105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species and invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/8/2006. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is a "buffer" as set forth in the instant claim 1. The essential elements of the instant claim 1 are: (1) an ionizable pharmaceutical agent, (2) a buffer, (3) an excipient, (4) wherein the composition is

essentially sugar-free. Since the instant claim 43 is dependent on claim 1 (buffer required), the examiner respectfully submits that it omits an essential element.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 15-16, 18-25, 27-28, 30-42 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,264,981 ('981).

'981 disclose pharmaceutical dosage forms comprising ionizable pharmaceutical agents, excipients, and buffers (Examples 2-3). As set forth in '981, the composition may be sugar-free (Example 2 – Table C) and can comprise buffer in an amount sufficient to maintain a portion of the agent in an ionized form (column 7, line 67 – column 8, line 17). As disclosed in Example 3, like the instant application, sorbitol may be used as the sugar substitute. As a well-known sugar substitute, the examiner respectfully asserts that sorbital would be bioequivalent to the sugar amount in a given oral transmucosal dosage form.

The buffer formulation in the '981 composition may comprise a combination of citric acid and di-sodium hydrogen phosphate buffered to a range of pH 6.0 (Example 3). The examiner respectfully submits that a pH of 6.0 reads on the limitation from

"about" 6.3 to 6.6 as presented in Claim 25. Like the instant claim set, the composition advanced by '981 may also comprise polyethylene glycol (Example 3). '981 disclose a number of pharmaceutical species suitable for use in the instant invention, including fentanyl (column 9, line 42; Table 1; Claims 27-28). Because the pKa of fentanyl is 7.3 (although it also changes on the basis of temperature – See Thurlkill et al.) and droperidol is 7.46 (See Table C), a "portion" of the agent would necessarily be in an ionized state upon dissolution of the dosage form in saliva. It should be noted that the dosage form disclosed by '981 can be formulated into a lollipop, lozenge, or chewing gum formulation (Claims 23-25).

The claims are therefore anticipated by US 6,264,981 ('981).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 11, 15-25, 27-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,264,981 ('981) in view of US 5,629,042 ('042) or US 2001/0029959 ('959).

'981 teach pharmaceutical dosage forms comprising ionizable pharmaceutical agents, excipients, and buffers (Examples 2-3). As set forth in '981, the composition may be sugar-free (Example 2 – Table C) and can comprise buffer in an amount sufficient to maintain a portion of the agent in an ionized form (column 7, line 67 – column 8, line 17). As taught in Example 3, like the instant application, sorbitol may be used as the sugar substitute. As a well-known sugar substitute, the examiner respectfully asserts that sorbital would be bioequivalent to the sugar amount in a given oral transmucosal dosage form.

The buffer formulation in the '981 composition may comprise a combination of citric acid and di-sodium hydrogen phosphate buffered to a range of pH 6.0 (Example 3). The examiner respectfully submits that a pH of 6.0 reads on the limitation from "about" 6.3 to 6.6 as presented in Claim 25. Like the instant claim set, the composition advanced by '981 may also comprise polyethylene glycol (Example 3). '981 teach a number of pharmaceutical species suitable for use in the instant invention, including fentanyl (column 9, line 42; Table 1; Claims 27-28). Because, as set forth in '981, fentanyl is a suitable active agent for use in the dosage form, one of ordinary skill in the art would have been motivated to use fentanyl as the active agent in the dosage forms

(Like table C, for example) advanced by '981. Based on the teachings of '981, there is a reasonable expectation that a dosage form, such as the one set forth in Table C, comprising fentanyl would have the ability to act as an effective oral transmucosal delivery device. As such, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate fentanyl into the dosage forms advanced by '981. Moreover, because the pKa of fentanyl is 7.3 (although it also changes on the basis of temperature – See Thurlkill et al.) and droperidol is 7.46 (See Table C), a "portion" of the agent would necessarily be in an ionized state upon dissolution of the dosage form in saliva. It should be noted that the dosage form disclosed by '981 can be formulated into a lollipop, lozenge, or chewing gum formulation (Claims 23-25).

'981 does not teach a dosage form comprising isomalt. However, both '042 and '959 teach the use of isomalt as an effective sugar substitute (Claim 15 of '042 and Example 6 of '959). Moreover, both '042 and '959 teach the equivalence of isomalt and sorbitol and further teach the use of both ingredients in the preparation of hard candies (Claim 15 of '042 and Example 6 of '959). Because, as confirmed by both '042 and '959, isomalt is an effective sugar-substitute, one of ordinary skill in the art would have been motivated to use isomalt in the sugar-free dosage form advanced by '981. Based on the teachings of both '042 and '959, there is a reasonable expectation that the substitution of isomalt, a well-known sugar substitute, for sorbitol in the composition of '981 would result in an effective sugar-free oral dosage form. As such, it would have

been obvious to one of ordinary skill in the art at the time the invention was made to use isomalt to the composition proposed by '981 in view of the teachings of both '042 and '959.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David L. Vanik whose telephone number is (571) 272-3104. The examiner can normally be reached on Monday-Friday 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Vanik, Ph.D.
Art Unit 1615

6/19/06

CARLOS A. AZPURU
PRIMARY EXAMINER
GROUP 1500